Using nitrofurantoin while breastfeeding a newborn

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Abstract

Question My patient has a urinary tract infection and is currently breastfeeding. Her son is only 3 weeks old. Is nitrofurantoin a safe antibiotic for treatment?

Answer The use of nitrofurantoin in breastfeeding mothers is generally safe, as only small amounts transfer into the breast milk. Despite the lack of documented reports, there is a risk of hemolytic anemia in all newborns exposed to nitrofurantoin owing to their glutathione instability, especially in infants with glucose-6-phosphate dehydrogenase deficiency. Although some suggest that nitrofurantoin be avoided in infants younger than 1 month, studies have noted that glutathione stability might be established by the eighth day of life. In infants younger than 1 month, an alternative antibiotic might be preferred; however, if an alternative were not available, the use of nitrofurantoin would not be a reason to avoid breastfeeding. In any such case the suckling infant should be monitored by his or her physician.

La nitrofurantoïne durant l'allaitement d'un nouveau-né

Résumé

Question Ma patiente souffre d'une infection des voies urinaires et allaite actuellement. Son fils n'est âgé que de 3 semaines. La nitrofurantoïne est-elle un antibiotique sécuritaire comme traitement?

Réponse L'utilisation de la nitrofurantoïne par des mères qui allaitent est généralement sécuritaire, car seulement de petites quantités passent dans le lait maternel. Malgré la rareté des rapports documentés, il y a un risque d'anémie hémolytique chez tous les nouveau-nés exposés à la nitrofurantoïne en raison de l'instabilité de leur glutathion, surtout chez ceux ayant une insuffisance en glucose-6-phosphate déshydrogénase. Quoique certains fassent valoir qu'il faudrait éviter la nitrofurantoïne chez des nourrissons de moins de 1 mois, des études ont permis de constater que la stabilité du glutathion pourrait être établie dès le huitième jour de vie. Si le nourrisson a moins de 1 mois, un autre antibiotique pourrait être envisagé; toutefois, si une autre option n'était pas disponible, l'utilisation de la nitrofurantoïne ne serait pas une raison pour éviter l'allaitement maternel. Dans un tel cas, l'enfant allaité devrait être surveillé par son médecin.

Urinary tract infections in the 30 days postpartum have been reported to occur at rates of 2.8% following cesarean section and 1.6% following vaginal birth.[1]

Nitrofurantoin is an antibiotic that has bactericidal activity against common urinary pathogens. Although its mechanism of action is not entirely clear, it is thought to inhibit several bacterial enzyme systems and interfere with bacterial metabolism and cell-wall synthesis.[2] It is detected at high levels in the urine; however, levels in plasma and whole blood are usually low and often undetectable.[2]

When considering the safety of taking medications while breastfeeding, an infant's exposure to the medication via breast milk is estimated by calculating the weight-adjusted dose, also referred to as the *relative infant dose*. A dose of less than 10% of the maternal weight–adjusted dose is generally considered less likely to increase the risk of adverse effects above that in an infant who is receiving the drug for therapeutic indications.[3]

Human studies in breast milk

Nitrofurantoin is actively transported into breast milk, likely through the BCRP (breast cancer resistance protein) transporter.[4] Older studies suggest that nitrofurantoin concentrations in breast milk are low, although the reported values are inconsistent. Two studies reported undetectable levels in breast milk—one in which 20 women took 100-mg doses 4 times a day,[5] another in which 5 women each took a single 100-mg dose.[6] In the latter study, an additional 2 of 4 women also had undetectable levels in breast milk following a 200-mg dose. However, the other 2 women had relative infant doses of 1.3% and 2.25%.[6] A 1990 study also reported less than 0.12% and 0.29% of the maternal dose in breast milk 6 hours after the fourth doses of 50 mg and 100 mg of nitrofurantoin, respectively.[7] In a more recent prospective single-dose pharmacokinetic human study, 4 healthy lactating women 8 to 26 weeks postpartum were each

administered a single 100-mg dose of nitrofurantoin. A mean milk concentration of 1.3 mg/L was reported. The authors suggest that the relative infant dose would be about 0.2 mg/kg, or 6% of the maternal dose per day.[8] Hence, these studies all indicate that nitrofurantoin's relative infant dose is less than 10% of the maternal dose and is therefore compatible with breastfeeding.

The only potential concern in the infant is diarrhea, which was reported by 2 of 6 nursing mothers following nitrofurantoin use in a prospective follow-up study conducted by Motherisk.[9]

Hemolytic anemia

There is a theoretical risk of hemolytic anemia in all newborns with exposure to nitrofurantoin owing to glutathione instability as a result of their immature erythrocyte enzyme systems.[2] Therefore, some have suggested that mothers exposed to nitrofurantoin should avoid breastfeeding infants younger than 1 month,[10,11] especially those infants with hyperbilirubinemia.[11] This might be a conservative recommendation, as studies have shown that this phenomenon might be transient.[12-14] In a follow-up study of term infants, the glutathione instability had normalized by the eighth day of life.[15] In a serial estimation of glutathione stability in preterm infants, such a finding was also observed.[16] Nevertheless, a similar concern might also be valid among infants, regardless of age, with an absolute or relative glucose-6-phosphate dehydrogenase (G6PD) deficiency.[17] Such deficiencies are commonly observed in eastern Mediterranean (eg, in those of Sardinian, Italian, Greek, or Jewish ethnicity), African, and Southeast Asian populations.[18] However, there are no published case reports of hemolytic anemia in infants caused by exposure to nitrofurantoin in breast milk.

Conclusion

Although nitrofurantoin might be actively excreted into breast milk, it is present in low amounts, with a maximum relative infant dose documented in the literature of 6%.[8] Some have suggested a theoretical risk of hemolytic anemia in infants younger than 1 month owing to glutathione instability. However, this appears to be a conservative view, as studies have reported normalization of this phenomenon by the eighth day of life in both term and preterm infants. Those with G6PD deficiencies, on the other hand, might be at risk regardless of age. Nevertheless, there have been no reported cases of complications in either at-risk group. If this is a concern for the patient or clinician, an alternative antibiotic might be prescribed. However, if the infant is older than 8 days and is unlikely to have a G6PD deficiency, then the use of nitrofurantoin might not be a reason to avoid breastfeeding.

Competing interests
None declared

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